Patient perceptions of the Raynaud's Condition Score diary provide insight into its performance in clinical trials of Raynaud's phenomenon

John D Pauling BMedSci BMBS PhD FRCP [1,2], Lesley A Saketkoo MD MPH [3-5] & Robyn T Domsic MD MPH [6]

[1] Royal National Hospital for Rheumatic Diseases (at Royal United Hospitals), Bath, UK

[2] Department of Pharmacy and Pharmacology, University of Bath, Bath, UK

[3] Tulane University School of Medicine, Lung Center, New Orleans, LA, US

[4] Scleroderma and Sarcoidsosis Patient Care and Research Center, New Orleans, LA, US

[5] University Medical Center Comprehensive Pulmonary Hypertension Center, New Orleans, LA, US

[6] University of Pittsburgh Medical Center, Pittsburgh, PA

Financial support: This work was undertaken using grant support from the Scleroderma Clinical Trials Consortium

Corresponding Author:

Dr John D Pauling BMedSci BMBS PhD FRCP

Senior Lecturer & Consultant Rheumatologist

Royal National Hospital for Rheumatic Diseases,

Royal United Hospitals,

Upper Borough Walls, Bath, BA1 1RL

Tel: (0044) 1225 473 468 Fax: (0044) 1225 473 452 JohnPauling@nhs.net

Disclsoures: None of the authors have any disclosures relevant to the content of this work.

The recent report by Denton et al. [1] adds to previous well-designed negative placebo-controlled clinical trials of Raynaud's phenomenon (RP) in systemic sclerosis (SSc). The primary endpoint was the weekly average number of RP attacks, with secondary endpoints including daily RP attack duration and RP severity (the single-item Raynaud's Condition Score [RCS]), that together comprise the RCS diary. The accompanying editorial, provides insightful suppositions of factors contributing to the disappointing performance of the RCS diary in clinical trials [2]. Given the lack of studies exploring patient attitudes towards the RCS diary, we investigated patient perceptions of the RCS diary. Twenty-one patients fulfilling the 2013 ACR/EULAR classification criteria for SSc from Bath (UK), New Orleans (US) and Pittsburgh (US) received training on completion of the RCS diary. Participants received a sealed envelope containing a quantitative and qualitative questionnaire (online supplement) along with instructions to only complete the survey after completion of the 2-week RCS diary. The survey comprised four sections examining (i) ease of completion; (ii) factors influencing diary returns; (iii) ranking of factors used to derive the RCS; and (iv) a qualitative survey examining strengths, limitations and potential for improvement. The study received ethics approval at each site with all patients providing consent. Most patients (11, 52%) found the diary easy to complete, with only 1 considering it a significant burden. Seven (33%) patients reported not recording all RP attacks. Most significantly, the majority (13, 62%) felt the number of RP attacks was unreflective of RP activity due to efforts taken to avoid attacks. Most subjects (16, 76%) reported difficulty recording the duration of attacks and the majority (13, 62%) felt duration of attacks was under-estimated by efforts taken to ameliorate symptoms. When asked which factors influenced the overall RCS, the highest mean ranked factors (in descending order) were the duration of attacks, inability to use hands, inability to perform other activities and number of attacks. Pain, numbness, burning and tingling were the lowest mean ranked factors. The qualitative survey confirmed ease of completion (Quotation [Q] 1, Table 1) although the concept of RP "attacks" was not shared by all (Q2). The diary helps subjects to focus on RP symptoms, although this may result in altered behaviour (Q3-4). Patients do not document all attacks (Q5-6)

and report frustration at an inability to capture relevant contributing external factors (Q7-8); particularly triggers and behavioural methods that directly influence diary returns (Q9). Suggestions included capturing emotional distress (Q10), recording circumstances surrounding attacks (Q11) and the development of wearable devices for remote monitoring (Q12). The patient experiences of the RCS diary captured in this study provide insight on its performance in clinical trials and could be used to support the development of novel approaches to assessing SSc-RP. The RCS diary is not over-burdensome but patients do not report all attacks and have difficulty recording duration of attacks. The RCS diary does not allow for the considerable efforts taken by patients to avoid or ameliorate symptoms and may not accurately reflect the true severity and impact of SSc-RP.

Table 1. Quotations from qualitative survey evaluating patient experiences of RCS diary

Q	Supporting quotation
1	It was fairly easy to complete
2	I am still not 100% sure that I know what an "ATTACK" is and make my assessment on how cold my hands are.
3	It made me more aware of attacks, made me look at my hands in different situations and if I needed to, I could do something about getting my hands back to normal circulation
4	It made me more aware of the triggers. I am convinced that change and stress are significant
5	Some of my Raynaud's attacks were so insignificant that they weren't worth reporting. I put these dates down as having no attacks that day
6	I know I had several smaller attacks that I did not record because they were too short
7	I felt I had to make 0 on the RCS but it didn't capture all of the inconvenient...things I had to do on those days to avoid having any attacks (or) what I was doing when I had attacks.
8	(The RCS diary) Did not take into account what I was doing that day. Was I outside more? Did I need to use my hands in colder environments?
9	Duration is so subjective I feel….Most long durations for me are when I'm out of my house and don't respond promptly with heated pillows etc."
10	Consider adding a question to identify the effect on the person's emotional well-being"
11	I think more info(rmation) is required....i.e. what you were doing at the time, what the temperature was like at the time, or what was causing the stress at the time.
12	I think in order to get an accurate number of attacks... I feel you need some sort of monitor to register the attacks as they happen .... I don't know if the diaries really tells all!

References

1. Denton, C.P., et al., Efficacy and Safety of Selexipag in Adults With Raynaud's Phenomenon Secondary to Systemic Sclerosis: A Randomized, Placebo-Controlled, Phase II Study. Arthritis Rheumatol 2017;69(12):2370-2379.

2. Seibold, J.R. and F.M. Wigley, Editorial: Clinical Trials in Raynaud's Phenomenon: A Spoonful of Sugar (Pill) Makes the Medicine Go Down (in Flames). Arthritis Rheumatol 2017;69(12):2256-2258.